Ciliary Body Thickness and the Relationship to Refractive Error and Accommodative Function in Adults

Thesis

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Abstract

The purpose of this study was to determine the relationships among ciliary body thickness, anterior scleral thickness, accommodative lag, and refractive error in adults as well as the difference between nasal and temporal ciliary body thickness.

Subjects with varying refractive error (range: −11.03 to +3.13 D) were recruited. Cycloplegic refractive error, axial length, accommodative lag (4.00-D stimulus), and ciliary body thickness (CBT2, CBT3) and anterior scleral thickness (AST2) at 2 and 3 mm posterior to the scleral spur were measured. Repeated measures regression models were used to define the relationship between CBT2, CBT3 and refractive error, axial length, or accommodative lag, and also AST2 and refractive error or axial length. A Bland-Altman analysis was utilized to determine the difference between nasal and temporal ciliary body thickness.

The relationships between CBT2 and CBT3 and refractive error were statistically significant (p = 0.04 and 0.02 respectively). The relationships between CBT2 and CBT3 and axial length were statistically significant (p = 0.01 and 0.002 respectively). No relationship was found between AST2 and refractive
error or between AST2 and axial length (all p > 0.05). The relationship between ciliary body thickness and accommodative lag was not significant at any measurement point.

The ciliary body was thicker in patients with increasing myopia and increasing axial lengths. Further studies are needed to determine if thicker ciliary bodies are related to the etiology of myopia and to determine if differences in the etiology exist for low-to-moderate myopia as opposed to high myopia.
Dedication

I dedicate this thesis to my family, friends and co-workers.

It was through their constant support this work was possible.
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Fields of Study

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Chapter 1: Introduction

1.1 Introduction

Recent research has begun to investigate the relationship between the structure and function of the ciliary body and how these relate to the development and progression of myopia. The following is a summary of the research relating to the characteristics of myopia, theories of etiology, prevention and treatment. This following study will concentrate on the ciliary body and the relationship between its structure and function and refractive error in adults.

1.2 Prevalence

It has previously been estimated that 25% of the population in the United States has a myopic refractive error. The National Health and Nutrition Examination Survey completed a survey between 1999 and 2004 to describe the prevalence of refractive error in the United States. They found myopia to be prevalent in 33.1% of the population and more common among females than
males. They also acknowledged myopia being more common in persons under the age of 60. As disquieting as these numbers are in the United States, there is an even greater prevalence of myopic refractive error in those persons of Asian descent. A study by Lin and co-workers reported that 84% of 16 to 18 year old Taiwanese school children have a myopia. Even more alarming among those of Asian descent is that the rate the prevalence of myopia is increasing. A thirteen-year longitudinal study was done and found that the prevalence of myopia increased from 49.3% to 65.6% in 17 year-olds. Given this growing number of effected persons, the etiology of myopia continues to be a widely debated topic.

1.3 How the myopic eye differs from emmetropic eye

The etiology of myopia is not completely understood, but there have been reports of distinct differences between the emmetropic and myopic eye which can explain the optical ramifications of myopia. Longer axial lengths and myopic refractive error have long been associated, and the increased axial length results in an optical focus that is anterior to the retina. Even with this strong association, an axial length of certain proportion does not always equal the same amount of refractive error from person to person. Sorsby proposed two models of myopia; low-to-moderate levels of myopia resulting from a mismatch in the optical components of the eyes while higher levels of myopia were more strongly associated with increased axial length. In either case of myopia, globe shape
and the structural components of the eye appear to play a role in the
development of this condition.

There have been several proposed causes of differences in globe shape. Investigators in the Collaborative Longitudinal Evaluation of Ethnicity and Refractive Error (CLEERE) Study have suggested the prolate shape of the eye is due to an equatorial growth restriction. Atchison and co-workers have also made several proposals involving myopia and the shape of the globe based on MRI data. They suggested the increase in axial length may be caused by a constriction of the orbital walls in the horizontal direction as opposed to the axial direction. Their report discussed two models for globe shape in the myopic eye, an axial elongation model and a global expansion model, acknowledging that myopia is not fully described by either model. Logan and co-workers in 2004 found there to be more growth in the axial direction when compared to equatorial expansion in both White and Taiwanese-Chinese subjects with increasing myopia using A-scan ultrasonography.

1.4 Genetics

Since the advent of the genome mapping, many diseases have been confirmed to have a genetic component and myopia is no exception. Studies have shown familial connections regarding myopia; however, not all varieties of myopia have these genetic connections. Sorsby was the one of the first to
suggest two different models of myopia and genetic mapping seems to confirm these suspicions of different myopic varieties. Myopia is now being considered as a multi-factorial disease with no clearly defined cause, but there have been several studies pinpointing genetic loci related to higher levels of myopia.\textsuperscript{12-14} Juvenile or late-onset myopia, however, does not share these genetic loci discussed previously and has more of an environmental component.\textsuperscript{11, 15}

1.5 Pathological vs. Juvenile Onset

Pathological myopia, juvenile-onset myopia, and late-onset myopia each have tendencies toward certain characteristics. Juvenile or late-onset myopia tends to manifest as decreased visual acuity between the ages of 9 and 11 years.\textsuperscript{16} Pathological myopia tends to be quantified by a refractive error of −6.00 D or more myopic. It can be distinguished from juvenile or late-onset myopia by an earlier age of onset or higher amounts of refractive error, and it is often accompanied by structural abnormalities of the posterior pole such as optic nerve head changes, staphyloma, retinal and vitreous degenerations, as well as retinal breaks and detachments.\textsuperscript{17} As discussed earlier, the pathological form of myopia has a greater genetic component.

1.6 Theories of the Etiology of Myopia
Animal models have been used as a means of better understanding the process of axial elongation and the mechanism behind it. Animal models have shown a link between axial hyperopic defocus and the development of myopia in both chickens and rhesus monkeys\textsuperscript{18-22}; however, these models have deficits when translating to the human due to structural differences of the eyes. The models do, however, provide a known stimulus which results in myopic growth.

Because of the association between hyperopic defocus and myopia in animal models, studies have sought to find an association between near work and myopia. In order to maintain focus on words at a close distance, the human accommodative system needs to be in a state of constant contraction. It is when this system is either inaccurate or unable to maintain this accommodative state that a state of hyperopic defocus occurs, possibly stimulating the growth of the eye in the axial direction. Myopia has been found to be accompanied by a reduced accommodative state in childhood and late-onset myopia.\textsuperscript{23-26} Whether or not the reduced accommodative response seen in these subjects is a result of the changes the eye undergoes during development of myopia or whether it is a cause of myopia continues to be debated.

1.7 Accommodative Lag and AC/A Ratio in Myopia

Because of the known reduction in accommodative accuracy in the already myopic subject, there have been several studies investigating whether or
not this phenomenon proceeds or accompanies the onset of myopia. Gwiazda and co-workers evaluated 80 children over a three year study and reported that the became-myopic children had an increased accommodative lag and elevated AC/A ratio at least two years before the onset of myopia. Contrary to this finding, Mutti and co-workers in the CLEERE study found no substantial differences accommodative lag between emmetropic children and children who later became myopic suggesting accommodative lag may be a consequence rather than a cause of myopia. The CLEERE investigators suggest several explanations for why lag accompanies the onset of myopia. Disuse of accommodation due to uncorrected refractive error, enlarged depth of field, increased number of higher order aberrations and blur adaptation all have theoretical basis, but none can fully explain the substantial lag that is present several years after the correction of myopia. The idea that accommodative lag is a result of the development of myopia rather than the cause has also been found in marmosets, with the marmosets developing accommodative dysfunction after myopia was experimentally induced. Reduced accommodation does not always seem to be present in the myopic subject, however. There have been several reports of reduced accommodative ability with myopia progression followed by an improvement in accommodative function once the myopic refractive error was stabilized and no longer progressing.

Two studies have reported that myopic children have an increased AC/A ratio. A study by Gwiazda and co-workers found an increased AC/A ratio in
myopic subjects and the AC/A ratios were found to be negatively correlated with age. They suggested a higher AC/A ratio is more likely to be present in the younger, progressing myopic subject as opposed to the older, stable myopic subject.\textsuperscript{31} The second study, by Mutti and co-workers, further discusses a hypothesis of why myopia onset results in low tonic accommodation, increased accommodative lag, and an elevated AC/A ratio.\textsuperscript{32} They suggested a deficit in the equatorial region of the eye, the ciliary body, the crystalline lens, and the choroid, and further hypothesize an equatorial growth restriction model of myopia.\textsuperscript{32} The equatorial growth restriction model could account for reduced equatorial stretch, resulting in a more prolate shape eye as well as a decreased ability of the ciliary body to accurately accommodate.

The studies described above investigated the accommodative response and AC/A in children with progressing myopia, but what about adult subjects who underwent the onset of myopia many years previously? The Study of the Progression of Adult Nearsightedness reported no difference in AC/A ratio between adults with progressing myopia and those with stable myopic refractive error, while lower amounts of accommodative lag were seen in those with progressing myopia.\textsuperscript{33} This is an interesting result given that studies of myopic children yield the opposite result.

Even with the interest in accommodative lag and AC/A ratio, few studies have been conducted to investigate the relationship between refractive error and the structure responsible for accommodation, the ciliary body. Little is known
about how the ciliary body varies among individuals with varying degrees of refractive error or how it varies in those with inaccurate accommodative systems. Schultz and co-workers used microfluctuations of accommodation as a measure of accommodative accuracy and attempted to address the role of the ciliary body in accommodative function using the Visante™ Anterior Segment OCT. They reported a tendency towards increased accuracy and stability of accommodation with increasing thickness of the ciliary body.34

Investigations of accommodative lag focus on central refractive error and accommodative accuracy, but the effect of peripheral refraction on the development of myopia is becoming an area of increasing interest. Various studies have found an association between central myopic refractive error and a peripheral relative refractive error in the more hyperopic direction.9, 35-37 Studies have also suggested this onset of peripheral relative hyperopia occurs before the onset of central myopia in both humans7, 38 and monkeys.39

1.8 Treatment of Myopia

Myopia has never been considered a life threatening disorder because of the readily available treatments using spectacles or contact lenses to allow affected persons to function completely normally in society. The economic burden of myopia in the United States has not been extensively studied. In 1990, it was estimated that 8.1 million dollars was spent on the correction of myopic refractive
error.\textsuperscript{40} That indicates a need to learn more about the cause of myopia to develop effective methods to slow or stop its progression.

As far as the prevention of myopia, it has recently been reported that an increased amount of time spent on outdoor activities has a protective effect against the development of myopia. Jones and co-workers found that children who partake in more hours of outdoor activity are less likely to be myopic than those who spend less time outdoors.\textsuperscript{41} A similar finding was described in Singaporean teenage children where outdoor activities were independently protective from myopia.\textsuperscript{42}

After the onset of myopia, studies have looked at various treatments to stop or slow the progression of myopia and to prevent the development of higher levels of myopia which can increase risk for further sight-threatening disorders. Considering the previously mentioned studies of myopia and accommodative lag, bifocals and progressive addition lenses have been tried as a method of slowing the development of myopia. They have been found to have a small effect on the progression of myopia\textsuperscript{43-45} especially in those demonstrating a higher amount of accommodative lag.\textsuperscript{46} Corneal Refractive Therapy has been shown to slow the progression of myopia as well.\textsuperscript{47} The mechanism underlying this treatment is thought to be related to the myopic peripheral refractive error that results outside of the treatment zone and acts as a stop signal for axial elongation. Finally, pirenzepine, a selective M1 muscarinic agonist, has been shown to slow the progression of myopia in human eyes in a two year clinical study.\textsuperscript{48}
1.9 Ciliary Body Anatomy

The ciliary body, the structure responsible for allowing the crystalline lens to change shape and accommodation, is made up of three arrangements of fibers; longitudinal, radial, and circular.\textsuperscript{49} The ciliary body is considered a smooth muscle; however, it differs from the smooth muscle found in the gastrointestinal tract by having several characteristics similar to that of striated muscle, including similar fast–fiber-like-structures and a rough endoplasmic reticulum.\textsuperscript{49} During accommodation, the ciliary body contracts inward and moves toward the anterior attachment point, the scleral spur,\textsuperscript{49} allowing for a release of tension on the zonules and a steepening of crystalline lens curvature. The ciliary body rapidly matures over the first two years of life, followed by a period of slowed, but continued growth past the age of six.\textsuperscript{50}

1.10 Ciliary Body and Myopia

The equatorial region of the eye is not a novel area of research concerning myopia. As indicated by the studies described above, this region of the eye has been thought to play a role in both the development of and subsequently, the treatment of myopia. Interestingly, the ciliary body, a structure involved in the process of accommodation, and its role in the progression of myopia has not
been well studied, probably because it has been historically difficult to view. In 2005, a small study by Oliveira and co-workers suggested an increase in ciliary body thickness in subjects with myopia as opposed to emmetropia and hyperopia.\textsuperscript{51} Another study found children with low-to-moderate amounts of myopia had increasingly thicker ciliary bodies with increasing amount of myopic refractive error.\textsuperscript{52} A third study looked at the differences in the thickness of the ciliary body between right and left eyes in subject with unilaterally high axial myopia, and they reported increased ciliary body thickness in the more myopic eye.\textsuperscript{53}

1.11 Summary

Even with the extensive research regarding myopia, many unknowns still remain regarding differences between pathological and juvenile-onset myopia, the exact cause of axial elongation, and the best mechanism to prevent further progression. The study by Oliveria introduced a new concept regarding the thickness of the ciliary body and its relationship to refractive error.\textsuperscript{51} The present study sought to replicate the previous study of myopia and ciliary body thickness using the Visante™ OCT Anterior Segment Optical Coherence Tomographer. The aims of the studies describe below are:

1. To investigate the relationship between ciliary body thickness and refractive error in adults;
2. To outline the relationship between ciliary body thickness and accommodative lag in adults with stable refractive error; and
3. To compare the thickness of the nasal and temporal ciliary body to determine if any differences in thickness are related to the overall thickness of the ciliary body.
Chapter 2: Methods

2.1 Subjects

Adults ages 18 to 39 years with various levels of refractive error were recruited through advertisements posted in and around The Ohio State University College of Optometry. Thus, the vast majority of subjects were faculty, staff, or students at the College. Subjects were required to have a best-spectacle-corrected visual acuity of 20/40 in each eye with no history of ocular disease, surgery or binocular vision anomalies. Subjects were excluded if they were using any topical ocular medications or systemic medications that might alter accommodative function. This study was conducted in accordance with the tenets of the Declaration of Helsinki. Following a presentation and discussion of the procedures and risks associated with the study, all subjects provided written consent. The study procedures and design were approved by the Institutional Review Board at The Ohio State University.

2.2 Measurements

All measurements were made on the right eye only. All cycloplegic
measurements were made with the following procedure. One drop of 0.5% proparacaine was instilled in the right eye followed by two drops of 1% tropicamide in each eye. The two drops of 1% tropicamide were instilled five minutes apart. Cycloplegic measurements were made 25 minutes after the last drop of tropicamide was instilled.

Refractive error was the mean spherical equivalent of five cycloplegic measurements taken with an autorefractor (binocular autorefractor/keratometer WR-5100K, Grand Seiko Co., Ltd., Hiroshima, Japan). Axial length measurements were the mean of three measurements made with an optical biometer (IOLMaster, Carl Zeiss Meditec). Accommodative lag was the mean of five spherical measurements obtained with a 4.00-D accommodative stimulus while subjects viewed a target of 20/100 letters through a Badal lens system attached to the open side of the autorefractor as previously described.²⁸

2.3 Visante™ Anterior Segment OCT Imaging of the Ciliary Body

The nasal and temporal ciliary body was imaged with an anterior segment OCT instrument (Visante™, Carl Zeiss Meditec) as previously described.⁵² Figure 1 is a sample image of the ciliary body obtained with the Visante™. Images of the nasal ciliary body were made while the subject fixated on a temporal target, followed by temporal ciliary body images taken as the subject fixated on a nasal target (Figure 2). The images were obtained in enhanced high
resolution corneal mode. Thickness measurements were made using a Matlab® (Mathworks, Natick) semi-automated algorithm.54 The scleral spur was identified in each image, and then ciliary body thickness was measured at positions 1 mm (CBT1), 2 mm (CBT2), and 3 mm (CBT3) posterior to the scleral spur (Figure 3). CBTmax was measured at the point of maximum ciliary body thickness. The intraocular bounds of the sclera and the ciliary pigmented epithelium were identified by the algorithm and served as the boundaries for the thickness measurements. The thickness of the sclera (AST2) overlying the ciliary body at CBT2 was also measured by the algorithm.

2.4 Statistical Analysis

For each ciliary body and scleral thickness measurement (CBT1, CBT2, CBT3, CBTMAX, and AST2) a repeated measures regression model was fitted to determine the relationship between the measurement and the following question predictors: cycloplegic spherical equivalent refractive error, axial length, and accommodative lag to a 4-D target. Each question predictor was fitted in an independent model. All models controlled for age and gender. For all models, continuous predictors were centered near their observed means (Table 1) to allow modeled intercepts to have a more meaningful interpretation, i.e., the value of the outcome at typical values of the predictors.
Models that were linear and quadratic in the question predictor were fitted. For example, the quadratic form of the model for CBT2 was:

\[
\text{CBT2}_{ij} = \text{Intercept} + A \cdot OC_{i} + B \cdot OC_{i}^2 + C \cdot \text{Gender}_i + D \cdot \text{Age}_i + \beta_i + \epsilon_{ij} \tag{1}
\]

In the model, the ocular component term (OC) is a placeholder for a question predictor. The linear model did not include the \( B \cdot OC_{i}^2 \) term. In the model, \( i \) indexes the subject and \( j \) indexes the subject’s repeated ciliary body or scleral thickness measurement. The model has two random components, \( \beta \) and \( \epsilon \). The \( \beta \) term accommodates the correlation of within-subject repeated measures. The \( \epsilon \) term captures within-subject variability.

A Bland-Altman comparison\(^{55}\) was used to analyze the difference in thickness between the nasal and temporal ciliary body and whether this difference was related to the overall thickness of the ciliary body.
Chapter 3: Results

3.1 The relationship between ciliary body thickness and refractive error or axial length

The general characteristics of the subjects recruited for this study are shown in Table 1. Mean, standard deviation, and range of ciliary body thickness measurements are included in Table 1. The subjects had a wide range of refractive errors.

The relationship between CBT2 and refractive error (Table 2, Figure 4) was statistically significant, as was the relationship between CBT3 and refractive error (Table 2). Ciliary body thickness was greatest in those with moderate-to-high levels of myopia. Refractive error was not associated with CBT1 or CBTmax (Table 2). All models controlled for age and gender with neither having a statistically significant effect in any model of ciliary body thickness and refractive error (Table 2).

The relationship between CBT2 and axial length (Table 3, Figure 5) was statistically significant, as was the relationship between CBT3 and axial length (Table 3). Ciliary body thickness was greatest at moderate-to-high values of axial length. Axial length was not associated with CBT1 or CBTmax (Table 3)
3.2 Ciliary body thickness and accommodative lag

There was one subject with a negative accommodative lag value and a very thick ciliary body. This subject was removed from the analysis as an outlier. The relationship between accommodative lag and ciliary body thickness was not significant at any measurement point (Table 4, Figure 5).

3.3 Anterior scleral thickness and refractive error or axial length

There was no statistically significant relationship between AST2 and either refractive error (Table 5) or axial length (Table 6, Figure 6). In both models, females had thinner AST2 measurements than males (Table 5 and 6, all p < 0.03). Increasing age was also associated with thinner AST2 (Table 5 and 6, all p < 0.03).

3.4 Nasal and temporal ciliary body thickness comparison

Forty-one subjects, 68.3% female with a mean (±SD) age of 25.7 (±4.4 range: 19 to 39) were included in the analysis. Table 7 is a summary of nasal and temporal ciliary body thickness measurements. Table 8 is a Bland–Altman comparison \(^{55}\) of nasal and temporal thickness measurements. The nasal ciliary
body was significantly different from the temporal ciliary body thickness at the 1 mm and 2 mm positions but not at the 3 mm position. The difference between the nasal and temporal measurements; however, was not related to the mean for any thickness measurement as seen in the difference versus mean plot for CBTmax (Figure 8).
Chapter 4: Discussion

The present study found there to be a small but significant difference between the thickness of the nasal and temporal ciliary body at the positions 1 and 2 mm posterior to the scleral spur. While the nasal ciliary body was thicker than the temporal ciliary body, the difference in thickness was not related to the overall thickness of the ciliary body. This finding suggests that measurements with the Visante™ Anterior Segment OCT can be made on the nasal or temporal ciliary body in future studies of myopia and presbyopia.

These data also confirm a relationship between the ciliary body thickness and refractive error in young, pre-presbyopic, adults using a non-contact anterior segment OCT. The relationship is similar to that reported previously in adults\(^51, 53\) and in children.\(^52\) The relationship is significantly significant at locations 2 mm and 3 mm posterior to the nasal scleral spur.

This study differed from the study by Oliveira and co-workers\(^51\) in several ways. The previous study in adults utilized an ultrasound biomicroscope in order to visualize the temporal ciliary body, where the present study imaged the nasal ciliary body using the non-contact Visante™ Anterior Segment OCT. Another
important distinction between the two adult studies relates to the age of the adult subjects.

There are age-related changes of both the ciliary body and refractive error which could be responsible for an obscured relationship. Our samples varied greatly with respect to age. The previous study, by Oliveira and co-workers (2005), had a mean age of 51.8 years versus 25.1 years in our study. It has been reported the aging ciliary body undergoes several changes resulting in structural and functional changes. Structurally, the ciliary muscle shows atrophy and an increase in the amount of intracellular connective tissue with increasing age.\textsuperscript{56, 57}

Refractive error of aging populations can also undergo fluctuations due to various conditions involving the crystalline lens. In previous studies, it has been reported that subjects of middle age undergo a hyperopic shift that can be attributed to progressive presbyopia, biometric changes or both. Conversely, myopic increases due to nuclear sclerotic changes occur in elderly subjects.\textsuperscript{58, 59}

In spite of age related changes that may have existed in the previous study, the present study confirmed the linear relationship between ciliary body thickness and refractive error.

This study also confirmed a linear relationship between ciliary body thickness and axial length. This suggests that although the eye is increasing in axial length and stretching during the progression of myopia, the ciliary body undergoes a process of thickening. If the ciliary body thickens myopia (as this study and a previous study from this laboratory\textsuperscript{52} have found), one might think
that the sclera overlying the ciliary body might undergo changes as well. These data, however, do not support this hypothesis, as there was no association between scleral thickness and refractive error or axial length. This could indicate that different growth processes occur in the ciliary body and the anterior sclera; however, these data were from adults who may have environmentally-related scleral and conjunctival changes.\textsuperscript{60} These data do, however, indicate AST2 thins with age. A better measure of whether or not there is an association between anterior scleral thickness and myopia would be to evaluate the relationship in a longitudinal study of children who have not had environmental or age-related changes in the thickness of the sclera.

As mentioned above, Sorsby suggested two different mechanisms of myopic development separating pathological myopia from juvenile-onset myopia.\textsuperscript{6} Although there are known genetic variations associated with both pathological and juvenile-onset myopia,\textsuperscript{11-15} the results of the present study do not suggest differences in the ciliary body between these two refractive groups. One might speculate that the genetic variations occur such that there are changes in the ciliary body in all types of myopia, but the genetic variations in pathological myopia are more limited to the posterior sclera, which result in the pathological findings associated with high myopia.

Smooth muscle develops in such a way as to balance functional capacity and demand.\textsuperscript{61} In the eye, there is a balance between the expanding, stretching and thinning lumen and the thickening of the ciliary body in emmetropia. In the case
of the myopic eye, however, the stimulus of axial elongation causes such a rapid overall thinning, expansion and stretching, there is a resultant tension on the equatorial region from the thinning crystalline lens. This intense stress imposed on the smooth muscle system of the ciliary body possibly disrupts this balance and could result in a compensatory mechanism to try and overcome this system deficit and consequently the muscle hypertrophies. A hypertrophic response in smooth muscle elsewhere, such as the gastrointestinal system, has been found to result in a thickening of the muscle as well as reduced contractile properties.\textsuperscript{62}

Thus, if the ciliary muscle is hypertrophic, one might consider how the function of the ciliary body would be affected. If the contractile capabilities were reduced because of hypertrophy, it can be assumed that accommodation, brought about by the contraction of the ciliary muscle, would be affected. Myopia has long been associated with a reduced accommodative response in childhood and late-onset myopia.\textsuperscript{23-26}

Accommodative dysfunction, however, does not always seem to be present in the myopic subject. There have been several reports of reduced accommodative ability with myopia progression followed by improvement with the stabilization of the myopic refractive error.\textsuperscript{24, 30} This is interesting when considering the data from this study. We found that adult myopic subjects, with thicker ciliary body measurements, have an accommodative lag that is similar to emmetropes, or those subjects with thinner ciliary bodies.

The subjects in the present study, many of whom were students and
faculty at the Ohio State University College of Optometry, were aware of their refractive error status and reported little to no change in their spectacle or contact lens prescription within the last year. Assuming the majority of the myopic subjects were stable, these results agree with previous reports, i.e., individuals with stable myopic refractive error have a stabilization of accommodative lag. Nonetheless, with the present data, the estimated correlation between accommodative lag and CBT2 after adjusting for gender and age is 0.21. Assuming this is the true correlation, 182 subjects would be required to have had 80% power to see a significant regression slope. Thus, further investigation of this relationship is required, and we will continue to investigate this relationship as more data are collected. A histological study of the human ciliary body in myopia could investigate if the increased thickness of the ciliary body is due to an increased thickness of the ciliary muscle and whether there is hypertrophy of the ciliary muscle in myopic subjects. An investigation on how the ciliary body changes throughout childhood with the onset and progression of myopia and how accommodative function is related to these changes is warranted.

In conclusion, our study suggests differences in the structure of the ciliary body in subjects with increasingly higher myopic refractive error. Further studies should investigate the longitudinal structural changes in children who have yet to become myopic to see exactly when these changes occur and whether they
coincide with changes in refractive error. Changes in accommodation, scleral thickness, and axial length would all be parameters to measure to determine an association to changes in the ciliary body.
Figure 1. Example anterior segment OCT image showing the nasal ciliary body of a subject.
Figure 2. Images used in the comparison of thickness between the a) Nasal ciliary body and b) temporal ciliary body
Figure 3. Thickness measurements (pink lines- CBT1, CBT2, CBT3) of the ciliary body and sclera were obtained from the outline of the ciliary body (blue). The point of maximum thickness (CBTMax) is shown in yellow.
Figure 4. Model projections of the relationship between ciliary body thickness (CBT2) and cycloplegic, spherical equivalent refractive error in adults. The relationship was linear ($p = 0.04$).
Figure 5. Model projections of the relationship between ciliary body thickness (CBT2) and axial length in adults. The relationship was linear ($p = 0.01$).
Figure 6. A multiple regression model of the relationship between accommodative lag for a 4.00-D stimulus and ciliary body thickness (CBT2). The relationship was not statistically significant ($p = 0.10$).
Figure 7. Model projections of the relationship between anterior scleral thickness (AST2) and axial length in adults. The relationship was not statistically significant as a linear model or with a quadratic term (shown, p = 0.4).
Figure 8. Difference between nasal and temporal ciliary body thickness versus mean plot for CBTmax.
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>25.1</td>
<td>5.0</td>
<td>18.0</td>
<td>40.0</td>
</tr>
<tr>
<td>Refractive error (D)</td>
<td>−3.00</td>
<td>3.17</td>
<td>−10.93</td>
<td>+3.25</td>
</tr>
<tr>
<td>Axial length (mm)</td>
<td>24.9</td>
<td>1.4</td>
<td>22.4</td>
<td>27.6</td>
</tr>
<tr>
<td>CBT1 (mm)</td>
<td>1.16</td>
<td>0.07</td>
<td>1.03</td>
<td>1.37</td>
</tr>
<tr>
<td>CBT2 (mm)</td>
<td>0.83</td>
<td>0.12</td>
<td>0.60</td>
<td>1.13</td>
</tr>
<tr>
<td>CBT3 (mm)</td>
<td>0.50</td>
<td>0.11</td>
<td>0.28</td>
<td>0.78</td>
</tr>
<tr>
<td>CBTmax (mm)</td>
<td>1.19</td>
<td>0.07</td>
<td>1.05</td>
<td>1.40</td>
</tr>
<tr>
<td>AST2 (mm)</td>
<td>0.94</td>
<td>0.10</td>
<td>0.79</td>
<td>1.29</td>
</tr>
<tr>
<td>Accommodative lag (D)*</td>
<td>1.32</td>
<td>0.6</td>
<td>−1.20</td>
<td>2.5</td>
</tr>
</tbody>
</table>

*4.00-D stimulus
CBT1, CBT2, and CBT3 = ciliary body thickness 1 mm, 2 mm, and 3mm posterior to the scleral spur
CBTmax = maximal thickness of the ciliary body
AST2 = anterior scleral thickness 2 mm posterior to the scleral spur

**Table 1.** Demographic characteristics of the thickness versus refractive error study (N = 63)
<table>
<thead>
<tr>
<th>Predictor</th>
<th>Parameter</th>
<th>Estimate</th>
<th>p-value</th>
<th>Parameter</th>
<th>Estimate</th>
<th>p-value</th>
<th>Parameter</th>
<th>Estimate</th>
<th>p-value</th>
<th>Parameter</th>
<th>Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td></td>
<td>1182.2</td>
<td></td>
<td>875.4</td>
<td></td>
<td>583.9</td>
<td></td>
<td>1214.0</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Refractive Error†</td>
<td>0.1</td>
<td>17.2</td>
<td>0.04</td>
<td>−10.2</td>
<td>0.02</td>
<td>−11.0</td>
<td>0.2</td>
<td>3.8</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age‡</td>
<td>0.4</td>
<td>−1.5</td>
<td>0.8</td>
<td>−0.8</td>
<td>0.4</td>
<td>−2.3</td>
<td>0.5</td>
<td>−1.2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Female</td>
<td>0.4</td>
<td>17.2</td>
<td>0.2</td>
<td>−38.4</td>
<td>0.08</td>
<td>−50.6</td>
<td>0.7</td>
<td>7.3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† Centered at −3.00 D
‡Centered at 25 years

Table 2. Repeated measures regression model of the relationship between ciliary body thickness and cycloplegic, spherical equivalent refractive error
<table>
<thead>
<tr>
<th>Predictor</th>
<th>CBT1</th>
<th>CBT2</th>
<th>CBT3</th>
<th>CBTmax</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>p-value</td>
<td>Parameter Estimate</td>
<td>p-value</td>
<td>Parameter Estimate</td>
</tr>
<tr>
<td>Intercept</td>
<td></td>
<td>1190.3</td>
<td></td>
<td>875.5</td>
</tr>
<tr>
<td>Axial Length†</td>
<td>0.5</td>
<td>−4.7</td>
<td>0.01</td>
<td>26.8</td>
</tr>
<tr>
<td>Age ‡</td>
<td>0.4</td>
<td>−1.7</td>
<td>0.8</td>
<td>−0.9</td>
</tr>
<tr>
<td>Female</td>
<td>0.5</td>
<td>12.7</td>
<td>0.4</td>
<td>−28.4</td>
</tr>
</tbody>
</table>

†Centered at 25 mm
‡Centered at 25 years

**Table 3.** Repeated measures regression model of the relationship between ciliary body thickness and axial length
<table>
<thead>
<tr>
<th>Predictor</th>
<th>Parameter Estimate</th>
<th>Parameter Estimate</th>
<th>Parameter Estimate</th>
<th>Parameter Estimate</th>
<th>Parameter Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td>1196.3</td>
<td>869.5</td>
<td>556.7</td>
<td>1223.1</td>
<td></td>
</tr>
<tr>
<td>Accommodative Lag†</td>
<td>0.1</td>
<td>-30.3</td>
<td>0.1</td>
<td>-52.9</td>
<td>0.3</td>
</tr>
<tr>
<td>Age‡</td>
<td>0.4</td>
<td>-1.7</td>
<td>0.9</td>
<td>-0.6</td>
<td>0.7</td>
</tr>
<tr>
<td>Female</td>
<td>0.8</td>
<td>6.2</td>
<td>0.3</td>
<td>-33.2</td>
<td>0.1</td>
</tr>
</tbody>
</table>

† Centered at 1.3 D
‡ Centered at 25 years

**Table 4.** Repeated measures regression model of the relationship between ciliary body thickness and accommodative lag for a 4.00-D stimulus
<table>
<thead>
<tr>
<th>Predictor</th>
<th>p-value</th>
<th>Parameter Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td></td>
<td>1105.0</td>
</tr>
<tr>
<td>Refractive Error (centered at −3.00 D)</td>
<td>0.4</td>
<td>3.2</td>
</tr>
<tr>
<td>Age (centered at 25 years)</td>
<td>0.03</td>
<td>−5.2</td>
</tr>
<tr>
<td>Female</td>
<td>0.03</td>
<td>−53.8</td>
</tr>
</tbody>
</table>

**Table 5.** Repeated measures regression model of the relationship between anterior sclera thickness (AST2) and cycloplegic, spherical equivalent refractive error
<table>
<thead>
<tr>
<th>Predictor</th>
<th>p-value</th>
<th>Parameter Estimate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intercept</td>
<td></td>
<td>1106.6</td>
</tr>
<tr>
<td>Axial Length (centered at 25 mm)</td>
<td>0.4</td>
<td>-6.9</td>
</tr>
<tr>
<td>Age (centered at 25 years)</td>
<td>0.03</td>
<td>-5.2</td>
</tr>
<tr>
<td>Gender (Female=1, Male=0)</td>
<td>0.02</td>
<td>-56.9</td>
</tr>
</tbody>
</table>

**Table 6.** Repeated measures regression model of the relationship between anterior scleral thickness (AST2) and axial length
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mean</th>
<th>Standard Deviation</th>
<th>Minimum</th>
<th>Maximum</th>
</tr>
</thead>
<tbody>
<tr>
<td>Temporal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBT1</td>
<td>1.00</td>
<td>0.06</td>
<td>0.88</td>
<td>1.15</td>
</tr>
<tr>
<td>CBT2</td>
<td>0.77</td>
<td>0.12</td>
<td>0.49</td>
<td>1.01</td>
</tr>
<tr>
<td>CBT3</td>
<td>0.51</td>
<td>0.10</td>
<td>0.31</td>
<td>0.78</td>
</tr>
<tr>
<td>CBTmax</td>
<td>1.04</td>
<td>0.06</td>
<td>0.94</td>
<td>1.17</td>
</tr>
<tr>
<td>Nasal</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CBT1</td>
<td>1.15</td>
<td>0.08</td>
<td>1.03</td>
<td>1.37</td>
</tr>
<tr>
<td>CBT2</td>
<td>0.82</td>
<td>0.12</td>
<td>0.60</td>
<td>1.13</td>
</tr>
<tr>
<td>CBT3</td>
<td>0.48</td>
<td>0.11</td>
<td>0.28</td>
<td>0.80</td>
</tr>
<tr>
<td>CBTmax</td>
<td>1.18</td>
<td>0.07</td>
<td>1.05</td>
<td>1.40</td>
</tr>
</tbody>
</table>

**Table 7.** Summary of temporal and nasal ciliary body thickness measurements (n=41 subjects)
<table>
<thead>
<tr>
<th>Measurement</th>
<th>Mean of the Differences</th>
<th>Standard Deviation of the Differences</th>
<th>Limits of Agreement</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Lower Bound</td>
</tr>
<tr>
<td>CBT1</td>
<td>0.15</td>
<td>0.09</td>
<td>−0.03</td>
</tr>
<tr>
<td>CBT2</td>
<td>0.05</td>
<td>0.14</td>
<td>−0.24</td>
</tr>
<tr>
<td>CBT3</td>
<td>−0.03</td>
<td>0.10</td>
<td>−0.22</td>
</tr>
<tr>
<td>CBTmax</td>
<td>0.14</td>
<td>0.08</td>
<td>−0.02</td>
</tr>
</tbody>
</table>

*Table 8.* Bland-Altman analysis comparing ciliary body thickness measurements (nasal – temporal).
List of References


